REMARKS

The Claims

Claims 37-57 have been cancelled without prejudice or disclaimer.

New Claims 58-81 have been added. The new claims are fully supported by the specification and do not introduce new matter or raise new issues requiring further consideration and/or search. Specifically, support for recitation of an epitope comprising "at least a part of the amino acid sequence ... " is found at p. 46, lines 7-9 and Example 11 which discloses the use of OPGbp peptides as immunogens. Entry of the new claims is respectfully requested.

Claims 58-81 correspond to the subject matter of cancelled Claims 37-57 and any changes in the new claims were introduced solely to clarify the subject matter. For example, Claim 58 clarifies that an antibody binds to an OPG binding protein harboring an epitope which comprises at least part of the amino acid sequence of OPGbp of SEQ ID NO:37. Accordingly, any changes do not narrow the scope of the claimed subject matter.

Supplemental Information Disclosure Statement

Pursuant to 37 CFR 1.97, Applicant submits herewith a copy of a Supplemental Information Disclosure Statement. This statement was originally submitted to the Office by facsimile on February 13, 2001 to Examiner Garnett Draper, the Examiner charged with the case at the time. In a subsequent telephone interview, Examiner Regina DeBerry, the present Examiner on the case, indicated that the statement was not in the file. Accordingly, Applicant is resubmitting this statement to correct the inadvertent omission from the file. The supplemental IDS provides information relating to a judgment entered by the Patent Board of Appeals and Interferences of the United States Patent and Trademark Office adverse to U.S. Patent No. 5,843,678, which matured from U.S. Serial No. 08/842,842, and U.S. Serial No. 08/880,855, The present application claims benefit of priority of both the '842 and '855 applications. Applicant requests that the information contained therein be considered and made of record.

Rejections under 35 U.S.C. 112

Claims 37-57 are rejected under 35 U.S.C. 112, first paragraph, as the specification allegedly fails to enable the claimed subject matter. The Examiner argues that it would require undue experimentation to

make naturally occurring osteoprotegerin binding protein (hereafter OPGbp) variants for immunization to generate the claimed antibodies.

Applicant maintains that the specification is fully enabled for antibodies which bind to an epitope on an OPG binding protein. The application provides the structure of both murine and human OPGbp and methods for preparing the proteins. It would also be well within the capabilities of one skilled in the art to prepare variants, including naturally occurring variants, soluble forms and fragments of OPGbp as immunogens. Moreover, Example 11 provides detailed methods of preparing and screening antibodies which bind an epitope on an OPG binding protein. Thus the direction and guidance provided in the application together with the state of the art and the high level of skill enable one to produce the claimed antibodies without undue experimentation. Screening for antibodies having desired characteristics was clearly recognized as not requiring undue effort and was an undertaking that practitioners of antibody technology can and would do. *In re Wands* 8 USPQ2d 1406 (Fed. Cir. 1988). Accordingly, it would not have required undue effort to identify antibodies which bind to OPGbp, including soluble forms, fragments and naturally occurring variants thereof.

Applicant also reiterates the arguments in support of enablement set forth in the responses of September 21, 2001 and May 20, 2002.

In the Advisory Action dated June 17, 2002, the Examiner continues to allege that it would require undue experimentation to identify a naturally occurring variant of OGPbp. It is now argued that in order to isolate a gene encoding a naturally occurring variant of OPGbp, one would "have to use conditions of reduced stringency which would also pick up sequences that are not related to OPGbp (false positives)". The Examiner appears to assume that naturally occurring variants of OPGbp are so different in sequence from OPGbp that they cannot be distinguished from non-OPGbp sequences under stringent hybridization conditions. There is absolutely no basis for concluding that naturally occurring variants could not be isolated under conditions of stringent hybridization and the Examiner cites no scientific literature to support this allegation. To the contrary, the specification teaches the isolation of the human OPGbp nucleic acid sequence using a mouse OPGbp DNA probe hybridizing to human DNA under stringent conditions. Clearly, if it did not require undue experimentation to obtain human OPGbp DNA by hybridizing under stringent conditions with murine OPGbp DNA, it should not require undue experimentation to identify naturally occurring OPGbp variants in a similar manner.

In the Advisory Action, the Examiner further alleges that "once the [OPGbp] gene is expressed, one would still need to demonstrate that this variant protein has the same activity as OPG binding protein

... ", apparently because an antibody to a naturally occurring variant of OPGbp would be "useless if the variant does not have the same activity as OPGbp." Applicant disagrees.

The claims are directed to antibodies which are effective in inhibiting bone resorption. There is no limitation in the claim requiring that the level of bone resorption be the same for OPG binding proteins reactive with the antibodies. The utility of the claimed antibodies does not depend on whether a variant has the same activity as OPGbp, but merely whether it has an activity that is sufficient to show some level of bone resorption. Thus the claims are enabled even if a variant does not have the same activity as OPGbp. Applicant also notes that a number of assays known in the art and set forth in the specification were available to determine the level of bone resorption by OPGbp variants. It would not have required undue experimentation to identify OPGbp variants and determine their activity.

Claims 37-57 are rejected under 35 U.S.C. 112, first paragraph, as the specification allegedly lacks sufficient written description of the claimed antibodies. The Examiner argues that written description is lacking for an antibody which binds to a naturally occurring OPGbp variant because no such variants were disclosed.

Applicant reiterates the arguments set forth in the response of September 12, 2001 and May 20, 2002. The specification provides sufficient written description for an antibody which binds a naturally occurring variant of OPGbp based upon previously cited Federal Circuit case law and the written description guidelines from the United States Patent and Trademark Office.

CONCLUSION

Claims 58-81 are believed to be in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,

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